REMARKS

Claims 1-21 are pending. Claims 2, 10-16, 18, 19 and 21 are withdrawn from consideration. Claims 1, 3-9, 17 and 20 are rejected. An appendix with the rejected claims is attached for the Examiner's convenience.

Priority Claim

The specification has been amended to delete a claim of continuing status to U.S. application Serial No. 60/070,457 filed January 5, 1998. A new set of declarations is being prepared and will be submitted as soon as possible. The effective filing date for this application with the foregoing change in priority is the filing date of the instant application, namely, December 29, 1998.

I. Claim Status

Applicants previously restricted prosecution to claim 17 of Group IV and elected VEGF as the species for examination of generic claims 1, 3-9, 17 and 20.

At page 2 of the Office Action, the Examiner comments on Applicant's statement that notwithstanding its election of species, that should the prior art permit, it would also be entitled to generic claims. In so doing, the Examiner emphasizes that the claims would be "considered for allowance **provided that they are rewritten and commensurate in scope with the elected-allowed invention**." [*emphasis in Office Action*].

If the Examiner is taking the position that the broadest claim that can possibly issue in this case will be limited solely to the species VEGF, such a position is inconsistent with the rules regarding the election of species. As set forth at page 4 of the June 1, 2000 Office Action, the Examiner states that Applicant is required to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Such language is consistent with 37 C.F.R. 1.146 wherein it is stated that the Examiner may require the Applicant to elect a species of the invention to which the claim will be restricted if no claim to the genus is found to be allowable. Accordingly, should examination of the species VEGF result in a determination that such species is allowable, the Examiner should conduct an

additional search to determine if a generic claim is allowable. To do otherwise, *i.e.*, to limit an application to the species only, would be inconsistent with the rules and preclude the allowance of a generic claim to which Applicant would otherwise be entitled.

If, in fact, it is the Examiner's position that a generic claim will not be considered in this case, even if the VEGF species is allowable, Applicant requests that the record be so clarified so that the issue can be properly framed for appeal, if necessary.

II. Rejection Under 35 USC §112, 2d paragraph

Claims 1, 3-9, 17 and 20 have been rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Federal Circuit has stated the legal standard for determining whether a claim is indefinite is "whether one skilled in the art would understand the bounds of the claim when read in light of the specification . . . . If the claims read in light of the specification reasonably apprize those skilled in the art of the scope of the invention, Section 112 demands no more." *Miles Lab., Inc. v. Shandon, Inc.*, 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993). In determining if claims are indefinite, claim language is analyzed in light of the teachings of the prior art and in light of the particular application disclosure as it would be interpreted by one having ordinary skill in the art. *In re Moore*, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (CCPA 1971).

The Office Action states "[t]he claims are vague and indefinite as to the proportions or amounts of VEGF and duration of time necessary for achieving the expected results. Moreover, how is the end result monitored and what is manifested by the method?" Applicant respectfully submits that the claims, as read in light of the specification reasonably apprizes those skilled in the art of the scope of the invention.

First, the specification provides that the growth factors are usually used at concentrations of 1fg/ml to 1 mg/ml, and that concentrations of 1 to 100 ng/ml are normally sufficient. *See*, p. 5, line 34 - p. 6, line 2. Examples with specific concentrations used are also provided. *See*, p. 18,

line 31- p. 19, line 3; p. 21, lines 16-19. Moreover, simple titration experiments can be performed to determine the optimal concentration of a growth factor. *See,* p. 6, lines 2-3.

Second, specification provides guidance on the appropriate treatment times necessary for achieving the expected results. Appropriate treatment times for contacting the metanephric tissue *in vitro* prior to transplanting are provided. *See*, p. 8, lines 3-10. Furthermore, appropriate concentrations and treatment times for contacting the metanephric tissue *in vivo* after transplantation are provided in the examples. See, p. 17, lines 17-22; p. 18, lines 14-22.

The Examiner further objects that the claims are indefinite as to what is manifested by the method. However, the specification clearly states that "growth factor treatment of the metanephric tissue . . . enhances the development and functioning of the chimeric kidney." *See*, p.4, lines 20-22.

The Examiner also states that the claims are indefinite as to how the end result is monitored. The examples in the specification provides that inulin clearances and urine output are increased in the chimeric kidneys that were treated as provided in Applicant's claims. Therefore, the end result can be monitored by performing simple inulin clearance assays and/or measuring urine output. *See*, p. 15, lines 19 - p. 17, line 4; p. 18, lines 23-30; p. 19, lines 5-14; p. 20, lines 24-31 (the chimeric kidney that results is considered functional if inulin clearance is greater than or equal to 10% of normal).

Finally, the Examiner states that the term "such that" in claim 9 is "indefinite as to how? The critical method steps and/or observations are missing from the claim." It is permissible, however, for a method step to recite some condition or property without reciting in the claim every step necessary to achieve the condition or property, as long as the specification discloses, or a person skilled in the art knows, how to achieve the condition or property. *In re Roberts and Burch*, 176 USPQ 313 (CCPA 1973) ("The claims define the limits of the claimed invention, and it is the function of the specification to detail how this invention is to be practiced."). Here, claim 9 recites the condition that the growth-factors are present in the recipient's blood that circulates through the transplanted metanephric tissue. The specification discloses that condition can be achieved through "periodic injections of the growth factors in the vicinity of the transplant." *See,* p. 8, lines 26-29. Furthermore, a person skilled in the art would readily know of alternative

methods of administering the growth factors such that they are present in the recipient's blood that circulates through the transplant. *See*, p. 17, lines 17-19; p. 21, lines 12-15.

III. Rejection for Nonstatutory Double Patenting

Claims 1, 3-9, and 17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 5,976,524 ("the '524 patent"), in view of Robert, et al, American Physiological Society, pp. F744-753 (1996) ("Robert *et al.*"). Applicants respectfully traverse the rejection.

The Office Action states that Robert *et al.* teaches that "VEGF is a potent cell-specific mitogen, enhances cell migration – vasculogenesis as well." (quoting Robert, page 747.) The Office Action further quotes the following from Robert, p. F751, "we believe that in response to VEGF some of these cells also take up positions within vasculature –," to conclude that it would have been obvious to incorporate VEGF in the method steps of the '524 patent and expect improved results at the time of the invention.

To establish a prima facie case of nonstatutory-type double patenting, the Examiner's showing of obviousness must follow the analysis used to establish a prima facie case of obviousness under 35 U.S.C. 103. *In re Longi*, 759 F.2d 887, 225 USPQ 645, 651 (Fed. Cir. 1985); MPEP §804.

Moreover, "...the focus of any double patenting analysis necessarily is on the claims in the multiple patents or patent applications involved in the analysis." MPEP §804. The present claims are directed to treating metanephric tissue with a growth factor containing composition which is presently limited to VEGF. None of the claim elements found in the '524 patent are recited as claim elements in the claims of this application. As such, the claims are clearly distinct from the claims of the '524 patent. The grant of a patent on the pending claims therefore would not extend the term of the claims of the '524 patent.

Notwithstanding the foregoing, the '524 patent claims do not disclose or suggest that the administration of growth factors to the donor metanephric tissue, either *in vitro* prior to transplantation or *in vivo* during or subsequent to the transplantation or that such treatment would enhance the development and functioning of the resulting chimeric kidney.

The Examiner's reliance on Robert *et al.* does not buttress the Examiner's double patenting rejection. Moreover, even if the Examiner were presenting a 102(e)/103 rejection, the Robert *et al.* disclosure does not render the present claims unpatentable.

Preliminarily, it should be noted that the '524 patent does not reference VEGF or any other growth factor for metanephric development.

Robert *et al.* discloses that "the *coordinate expression* of VEGF and one of its receptors, flk-1, suggests a crucial role for this ligand/receptor pair in renal vascular development. Robert *et al.*, p. 747 (emphasis added); *see also,* Robert *et al.*, p. 748 ("The detection of both VEGF and flk-1 mRNAs in embryonic glomeruli also strongly suggests that the coordinated expression of these proteins regulates both the timing and location of glomerular capillary assembly."). To further test this hypothesis, Robert *et al.* studied the distribution of flk-1, in developing mouse kidneys. Robert *et al.* finds that flk-1 is expressed in glomeruli and microvessels and states his results are "consistent with proposals that flk-1 mediates endothelial differentiation and formation of vascular structures." Robert, p. F751.

While Robert *et al.* studied the distribution and location of flk-1, the reference does not disclose or suggest the administration of VEGF to transplanted metanephros. Moreover, Robert *et al.*'s emphasis on the *coordinate expression* of VEGF and flk-1 does not suggest that the administration of VEGF to the donor metanephric tissue, either in vitro prior to transplantation, or in vivo during or subsequent to the transplantation would enhance the development and functioning of the resulting chimeric kidney. Robert *et al.* also does not disclose the transplantation of metanephric tissue into a xenogenic host, or suggest how the coordinate expression of VEGF and flk-1 would impact the transplantation of metanephric tissue into a xenogenic host.

Finally, the '524 patent discloses that the origin of the glomerular blood vessels is extrametanephric. Therefore, the implanted metanephros becomes vascularized by the recipient's blood vessels, forming a functioning chimeric kidney. In contrast, Robert *et al.* teaches that the origin of renal glomerular and microvascular endothelium is probably from the donor graft material and not the recipient. *See,* Robert *et al.*, p. F744; F747; and F751. Robert *et al.*

therefore teaches away from the '524 patent, and it would not have been obvious to incorporate VEGF in the method of the '524 patent.

Applicants respectfully submit that each and every element of the claims is not disclosed in the cited art. Further, there is motivation or suggestion provided to modify or combine the disclosures. Finally, there is no basis to conclude that the skilled artisan would reasonably expect to successfully arrive at the claimed invention by following Robert *et al.* and the '524 patent.

Based on the foregoing, the rejections should be withdrawn

The Commissioner is authorized to charge any additional fees, including any extension fees, which may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our Order No. A-68752/RFT).

Respectfully submitted,

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